

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:	Reissue of U.S. Patent No. 6,114,397
Flack et al.	Issued: September 5, 2000
Application No. Unassigned	Art Unit: Unassigned
Filed: Herewith	Examiner: Unassigned
Assigned to: The United States of America as represented by the Secretary of the Department of Health and Human Services	
For:	GOSSYPOL FOR THE TREATMENT OF CANCER

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop Reissue  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Pursuant to 37 CFR 1.97 and 1.98, the references listed on the enclosed Form PTO-1449 and/or Substitute Form PTO-1449 ("Form 1449") are submitted for consideration by the Examiner in the examination of the above-identified patent application.

The full consideration of the references in their entirety by the Examiner is respectfully requested and encouraged. Also, it is respectfully requested that the references be entered into the record of the present application and that the Examiner place his or her initials in the appropriate area on the enclosed Form 1449, thereby indicating the Examiner's consideration of each of the references.

The submission of the references listed on the Form 1449 is for the purpose of providing a complete record and is not a concession that the references listed thereon are prior art to the invention claimed in the patent application. The right is expressly reserved to establish an invention date earlier than the above-identified filing date in order to remove any reference submitted herewith as prior art should it be deemed appropriate to do so.

Further, the submission of the references is not to be taken as a concession that any reference represents art that is relevant or analogous to the claimed invention. Accordingly, the right to argue that any reference is not properly within the scope of prior art relevant to an examination of the claims in the above-identified application is also expressly reserved.

The Information Disclosure Statement is being filed:

- ☒ **within** any one of the following time periods: (a) within three months of the filing date of a national application other than a continued prosecution application under 37 CFR 1.53(d); (b) within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 of an international application; (c) before the mailing date of a first Office Action on the merits; or (d) before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.
- ☐ **after** (a), (b), (c) or (d) above, but before the mailing date of a final action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and includes *one* of:
- ☐ the Statement under 37 CFR 1.97(e) (see "Statement under 37 CFR 1.97(e)" below).
- or*
- ☐ the fee of \$180 set forth in 37 CFR 1.17(p) (see "Fees" below).
- ☐ **after** the mailing date of a final action under 37 CFR 1.113 or a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and on or before payment of the issue fee, and includes the Statement under 37 CFR 1.97(e) (see "Statement under 37 CFR 1.97(e)" below), and the fee of \$180 as set forth in 37 CFR 1.17(p) (see "Fees" below).
- ☐ **after** the mailing date of a Notice of Allowance under 37 CFR 1.311, and on or before payment of the issue fee, and **within** thirty days of receiving each item of information contained in the Information Disclosure Statement, and includes the Statement under 37 CFR 1.704(d) (see "Statement under 37 CFR 1.704(d)" below), and the fee of \$180 as set forth in 37 CFR 1.17(p) (see "Fees" below).
- NOTE: This is for original applications except applications for a design patent, filed on or after May 29, 2000, wherein a paper containing only an Information Disclosure Statement in compliance with 37 CFR 1.97 and 1.98 is being filed.

#### Copies of the References

- ☒ Copies of the references listed on the enclosed Form 1449 are enclosed herewith. Attached to each reference not in the English language is a concise explanation of the relevance pursuant to 37 CFR 1.98(a)(3). An English-language equivalent/patent, or an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office is being submitted in lieu of a concise explanation of the relevance pursuant to 37 CFR 1.98(a)(3).
- ☐ A copy of the foreign search report is enclosed herewith.
- ☐ The references listed on the enclosed Form 1449 were previously identified in the parent application(s) of the present application, and copies of the references were furnished at that time. Accordingly, additional copies of the references are not

submitted herewith, so as not to burden the file with duplicate copies of references. The Examiner is respectfully requested to carefully review the references in accordance with the requirements set out in the Manual of Patent Examining Procedure. In accordance with 37 CFR 1.98(d), the details of the parent application(s) relied upon for an earlier filing date under 35 USC 120 in which copies of the references were previously furnished are set out below:

U.S. APPLICATIONS		Status ( <i>check one</i> )		
U.S. APPLICATIONS	U.S. FILING DATE	PATENTED	PENDING	ABANDONED
1.				
2.				
3.				

**Statement under 37 CFR 1.97(e)**

- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.
- ☐ The **undersigned** hereby states that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application, and, to the knowledge of the undersigned after making reasonable inquiry, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the Information Disclosure Statement.

**Statement under 37 CFR 1.704(d)**

- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and that this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.

**Fees**

- ☒ **No fee** is owed by the applicant(s).
- ☐ The **IDS Fee of \$180** under 37 CFR 1.17(p) is enclosed herewith.

**Method of Payment of Fees**

- ☐ Attached is a check in the amount of \$ .
- ☐ Charge Deposit Account No. 12-1216 in the amount of \$ . (A duplicate copy of this communication is enclosed for that purpose.)

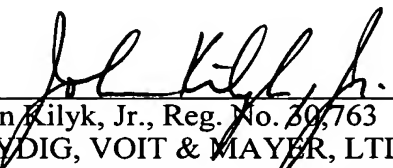
In re Appln. of Flack et al.  
Application No. Unassigned

**Authorization to Charge Additional Fees**

- ☒ If any additional fees are owed in connection with this communication, please charge Deposit Account No. 12-1216. (A duplicate copy of this communication is enclosed for that purpose.)

**Instructions as to Overpayment**

- ☒ Credit Account No. 12-1216.  
☐ Refund

  
\_\_\_\_\_  
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Date: March 22, 2004

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Substitute for form 1449A/B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)			<b>Complete if Known</b>		
			Application Number	Unassigned	
			Filing Date	February 6, 2004	
			First Named Inventor	Flack et al.	
			Group Art Unit	Unassigned	
			Examiner Name	Unassigned	
Sheet	1	of	3	Attorney Docket Number	225011

U.S. PATENT DOCUMENTS						
Examiner Initials	Doc. No.	U.S. Patent Document		Name of Patentee or Applicant	Date of Publication	Filing Date If Appropriate
		Application or Patent Number	Kind Code			
	AA	4,297,341		Waller et al.	Oct. 27, 1981	
	AB	5,026,726		Jagt et al.	June 25, 1991	
	AC	5,260,327	A	Kim et al.	Nov. 9, 1993	
	AD	5,759,837	A	Kuhajda et al.	June 2, 1998	
	AE	6,576,660	B1	Liao et al.	June 10, 2003	

FOREIGN PATENT DOCUMENTS								
Examiner Initials	Doc. No.	Foreign Patent Document			Name of Patentee or Applicant	Date of Publication	Translation	
		Office	Application or Patent Number	Kind Code			Yes	No**
	AF	JP	1-132542	A	TOOMEN:KK	May 25, 1989		X*

OTHER - NON PATENT LITERATURE DOCUMENTS								
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.					Translation	
							Yes	No**
	AG	BAND et al., "Antiproliferative Effect of Gossypol and Its Optical Isomers on Human Reproductive Cancer Cell Lines," <i>Gynecologic Oncology</i> , 32, 273-277 (1989)						
	AH	BAND et al., "Cytocidal Effects of Gossypol and Its Optical Isomers on Reproductive Cancer Cell Lines," <i>Gynecologic Oncologists</i> , 23 (2), 261 (1986)						
	AI	BENZ et al., "Biochemical Correlates of the Antitumor and Antimitochondrial Properties of Gossypol Enantiomers," <i>Molecular Pharmacology</i> , 37, 840-847 (1990)						
	AJ	BENZ et al., "Gossypol Enantiomers (+, -) Differentially Uncouple Tumor Mitochondria, Block Glutathione-S-Transferase Activity, and Inhibit Cellular Proliferation," <i>79<sup>th</sup> Annual Meeting of the American Association for Cancer Research, Proceedings</i> , 29, 322 (1988)						
	AK	BENZ et al., "Lactic Dehydrogenase Isozymers, <sup>31</sup> P Magnetic Resonance Spectroscopy, and In Vitro Antimitochondrial Tumor Toxicity with Gossypol and Rhodamine-123," <i>The Journal of Clinical Investigation</i> , 79 (2), 517-523 (1987)						
	AL	BENZ et al., "Selective Toxicity of Gossypol Against Epithelial Tumors and its Detection by Magnetic Resonance Spectroscopy," <i>Contraception</i> , 37 (3), 221-229 (1988)						
	AM	COTTON CELLULOSE CHEMISTR, "Gossypol prepn - from gossypol and anthranilate by alkaline hydrolysis of the anthranilate," SU 212245 (English abstract only) (1973)						X*
	AN	DE MARTINO et al., "Electron microscopic and biochemical studies of the effect of Gossypol on Ehrlich ascites tumor cells," <i>Caryologia</i> , 35, 114-115 (1982)						
	AO	DHALIWAL et al., "Cytogenetic Analysis of a Gossypol-Induced Murine Myxosarcoma," <i>Journal of the National Cancer Institute</i> , 78 (6), 1203-1209 (1987)						
	AP	FLACK et al., "Treatment of adrenocortical carcinoma with gossypol," <i>81<sup>st</sup> Proceedings of the American Association for Cancer Research</i> , 31, 198 (1990)						
	AQ	FLORIDI et al., "The Effect of the Association of Gossypol and Lonidamine on the Energy Metabolism of Ehrlich Ascites Tumor Cells," <i>Experimental and Molecular Pathology</i> , 38, 322-335 (1983)						
	AR	HAN et al., "Gossypol in the Treatment of Endometriosis and Uterine Myoma," <i>Contributions to Gynecology and Obstetrics</i> , 16, 268-270 (1987)						
	AS	HASPEL et al., "Cytocidal Effect of Gossypol on Cultured Murine Erythroleukemia Cells is Prevented by Serum Protein," <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 229 (1), 218-225 (1984)						

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			Filing Date	February 6, 2004	
			First Named Inventor	Flack et al.	
			Group Art Unit	Unassigned	
			Examiner Name	Unassigned	
Sheet	2	of	3	Attorney Docket Number	225011

#### OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation	
			Yes	No**
	A T	HU et al., "Gossypol Effects on Cultured Normal and Malignant Melanocytes," <i>In Vitro Cellular &amp; Developmental Biology</i> , 22 (10), 583-588 (1986)		
	A U	HUANG et al., "Resolution of Racemic Gossypol," <i>Journal of Ethnopharmacology</i> , 20, 13-20 (1987)		
	A V	JAROSZEWSKI et al., "Action of Gossypol and Rhodamine 123 on Wild Type and Multidrug-resistant MCF-7 Human Breast Cancer Cells: <sup>31</sup> P Nuclear Magnetic Resonance and Toxicity Studies," <i>Cancer Research</i> , 50, 6936-6943 (1990)		
	A W	JINGFANG et al., "of Gossypol in Mice, Rats and Human Tumor Cell Lines and Its Possible Mechanism," <i>Acta Academiae Medicinae Sinicae</i> , 8 (6), 486-489 (1986)		X*
	A X	JOLAD et al., "Tumor-Inhibitory Agent from <i>Montezuma speciosissima</i> (Malvaceae)," <i>Journal of Pharmaceutical Sciences</i> , 64 (11), 1889-1890 (1975)		
	A Y	JOSEPH et al., "Cytotoxicity of enantiomers of gossypol," <i>The British Journal of Cancer</i> , 54 (3), 511-513 (1986)		
	A Z	KAI et al., "Resolution of Racemic Gossypol," <i>Journal of the Chemical Society</i> , (3), 168-169 (1985)		
	B A	KENIRY et al., "The Effect of gossypol and 6-aminonicotinamide on tumor cell metabolism: A <sup>31</sup> P-Magnetic Resonance spectroscopic study," <i>Biochemical and Biophysical Research Communications</i> , 164 (2), 947-953 (1989)		
	B B	KENIRY et al., "Magnetic Resonance Spectroscopy (MRS) and Imaging (MRI) in the Evaluation of Tumor Growth and Chemotherapy Response," <i>Proceedings, 77<sup>th</sup> Annual Meeting of the American Association for Cancer Research</i> , 27, 384 (1986)		
	B C	KIM et al., "Comparative In Vitro Spermicidal Effects of ( ± )-Gossypol, ( + )-Gossypol, ( - )-Gossypol, and Gossypolone," <i>Contraception</i> , 30 (3), 253-259 (1984)		
	B D	KUZNEZOVA et al., "Measurement of Cytotoxic effects and anti-cancer properties of gossypol and its derivatives," <i>Pharmacol. Toxicol.</i> , 1-7 (1979) (English abstract only)		X*
	B E	MATLIN et al., "Large-Scale Resolution of Gossypol Enantiomers for Biological Evaluation," <i>Contraception</i> , 37 (3), 229-237 (1988)		
	B F	McSHEEHY et al., "Gossypol, a cytotoxic agent, may uncouple respiration of Ehrlich Ascites tumour cells," <i>BIOCHEMICAL SOCIETY TRANSACTIONS</i> , 16 (4), 616-617 (1988)		
	B G	MEILING, "Gossypol Treatment for Menopausal Functional Bleeding, Myoma of Uterus and Endometriosis—Preliminary Report," <i>Acta Academiae Medicinae Sinicae</i> , 2 (3), 168-170 (1980)		
	B H	NAYAK et al., "Induction of Sister Chromatid Exchanges and Chromosome Damage by Gossypol in Bone Marrow Cells of Mice," <i>Teratogenesis, Carcinogenesis, and Mutagenesis</i> , 6 (2), 83-91 (1986)		
	B I	OHUCHI et al., "Inhibition by gossypol of tumor promoter-induced arachidonic acid metabolism in rat peritoneal macrophages," <i>Biochimica et Biophysica Acta</i> , 971, 85-91 (1988)		
	B J	PIROGOV et al., "Postoperative Bronchopleural Complications in Combined Treatment of Pulmonary Cancer," <i>VOPROSY ONKOLOGII</i> , 20 (6), 24-28 (1974)		X*
	B K	QIAN et al., "Gossypol: A Potential Antifertility Agent for Males," <i>Annual Review of Pharmacological Toxicology</i> , 24, 329-360 (1984)		
	B L	RAO et al., "Antitumor effects of gossypol on murine tumors," <i>Cancer Chemotherapy. Pharmacology</i> , 15, 20-25 (1985)		
	B M	SAMPATH et al., "A Rapid Procedure for the Resolution of Racemic Gossypol," <i>Journal of the Chemical Society</i> , (9), 649-650 (1986)		

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			Yes	No**
	B N	TANPHAICHITR et al., "Direct Effect of Gossypol on TR-ST Cells: Perturbation of Rhodamine 123 Accumulation in Mitochondria," <i>Biology of Reproduction</i> , 31, 1049-1060 (1984)		
	B O	THOENES et al., "Cytotoxic Effects of Adriamycin, Bleomycin, Gossypol and Hydroxylanisol to Cultured Human Malignant Melanoma Cells," <i>Journal of Cancer Research and Clinical Oncology</i> , 113, S 46 (1987)		
	B P	TSO, "Gossypol Inhibits Ehrlich Ascites Tumor Cell Proliferation," <i>Cancer Letters</i> , 24, 257-261 (1984)		
	B Q	TUSZYNSKI et al., "Differential Cytotoxic Effect of Gossypol on Human Melanoma, Colon Carcinoma, and Other Tissue Culture Cell Lines," <i>CANCER RESEARCH</i> , 44, 768-771 (1984)		
	B R	VERMEL et al., "Antitumor Activity of Gossypol in Experiments on Transplanted Tumours," <i>Voprosy Oncologii</i> , 9 (12), 30-43 (1963)		X <sup>+</sup>
	B S	WANG et al., "Effect of Gossypol on DNA Synthesis and Cell Cycle Progression of Mammalian Cells <i>in Vitro</i> ," <i>Cancer Research</i> , 44, 35-38 (1984)		
	B T	WU et al., "An <i>in Vitro</i> and <i>in Vivo</i> Study of Antitumor Effects of Gossypol on Human SW-13 Adrenocortical Carcinoma," <i>Cancer Research</i> , 49, 3754-3758 (1989)		
	B U	WU et al., "In vitro antitumor activity of gossypol alone or in combination with amsacrine," <i>European Journal of Pharmacology</i> , 183 (2), 230 (1990)		
	B V	WU et al., "Pharmacokinetics of (±)-, (+)-, and (-)-gossypol in humans and dogs," <i>Clinical Pharmacology &amp; Therapeutics</i> , 39 (6), 613-618 (1986)		
	B W	XUEQING et al., "Clinical Observation and Experimental Study of Gossypol in Treatment of Dysfunctional Menorrhagia, Endometriosis and Fibromyoma of Uterus," <i>Chinese J. Integre. Trad. Western Med.</i> , 8, 197 & 216-217 (1988)		X <sup>+</sup>
	B X	YERUKHIMOV, "Treatment of Bladder Tumors with Gossypol and Ionol in Combination with Surgical Intervention," <i>VOPROSY ONKOLOGII</i> , 12 (2), 29-34 (1966)		X <sup>+</sup>
	B Y	YIKANG et al., "Studies on Resolution of Racemic Gossypol: Separation of Hexaacetates of S-1-Methylphenethylamino Derivative of (±) Gossypol," <i>Scientia Sinica</i> , 30 (3), 297-303 (1987)		
	B Z	YU, "Probing into the Mechanism of Action, Metabolism and Toxicity of Gossypol by Studying Its (+)- and (-)- Stereoisomers," <i>Journal of Ethnopharmacology</i> , 20, 65-78 (1987)		
	C A	ZHENG et al., "STUDIES ON THE RESOLUTION OF RACEMIC GOSSYPOL: IV. Use of Threo(-) or (+)-1-(p-Nitrophenyl)-1,3-Dihydroxypropylamine-2 as the Resolving Agent," <i>Acta Pharmaceutica Sinica</i> , 25 (6), 430-434 (1990)		X <sup>+</sup>

Examiner Signature		Date Considered	
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\* A concise statement of relevance is being submitted in lieu of a translation. 37 CFR 1.98(a)(3).

+ An English-language equivalent/patent, or an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office is being submitted in lieu of a concise explanation of relevance under 37 CFR 1.98(a)(3).